

REMARKS

The office action mailed on February 5, 2009 and the comments therein have been carefully considered. Applicants address each below.

I. Maintained Objection

The Examiner questions the date of the Genbank sequence submission as support of possession of the sequence before the priority date of the patent application. As further support that Applicants were in possession of the correct sequence at the priority date, Applicants submit sequence chromatograms from May - September, 1996 showing the regions of interest. *See Appendix A.* Applicants respectfully request reconsideration and correction of the sequence listing for accuracy.

II. New Objection to Specification

Amendments filed in 2002 are objected to under 35 U.S.C. 132(a). Applicants address each as listed in the office action:

p. 1, line 18 – please cancel addition of “assessing the risk of ovarian cancer”; Applicants note this is in line 20 not 18

p. 2, line 4 – please cancel replacement of “c-erbB1” with “EGFR/ErbB1”

p. 2, line 6 – replacement of “1991” with “1990” is a typographical correction of the reference year

p. 2, line 7 – replacement of “20” with “90” is a typographical correction of the reference volume

p. 2, line 15- please cancel addition of the sentence “In addition, alternatively spliced mRNA’s from the EGFR/ErBB1 gene also encode soluble forms of this receptor.”

p. 2, line 22 – typographical correction of reference name “Somat Cell Mol. Genet.”

p.2, line 22 – please cancel replacement of “*c-erbB1*” with “EGFR/ErbB1”

p.2, line 23 – please cancel replacement of “2.6-2.7” with “1.8-2.8”

p.2, line 24- please cancel replacement of “chicken and rat tissue” with “human, chicken, rat, and mouse tissues”

p.2, line 25 – please cancel replacement of “*supra*” with reference

p.3, line 11 – typographical correction of U.S. Patent No. 5,674,753, which relates to subject matter described in the text. U.S. Patent No. 5,674,763 does not relate to the disclosed subject matter.

p.4, line 9- typographical correction; “soluble epidermal growth factor receptors” is used throughout the specification, including p. 4, line 6 and the title of the application.

p.6, line 15- please cancel addition of “and/or sEGFR”

p. 6, line 19- please cancel addition of “and full-length”

p. 7, line 11- please cancel addition of “saliva, sputum, breast nipple aspirates”

p. 7, line 23- please cancel addition of “or decrease”

p. 7, line 25 – please cancel addition of “ligands, such as”

p. 8, line 1- please cancel addition of sentence “Alternatively, the method may be used to decrease the circulatory half-life of these ligands by allowing cells to remove sErbB1-ligand complexes from the circulation by endocytosis and intracellular membrane transport.”

p. 8, line 2- please cancel replacement of “increasing” with “altering”

p. 8, line 17 – please cancel addition of “and may play important roles in regulating development, wound healing, carcinogenesis, and tumor progression”

p. 9, line 8 – please cancel addition of “sEGFR”

p. 9, line 17 – please cancel addition of “EGFR”

p. 9, line 19 – please cancel addition of “sErbB1” and “EGFR”

p. 9, line 20 – please cancel addition of “sErbB1”

p. 11, line 8 – amend to female (n=144) and male (n=88) as supported in Example VI generally and specifically p. 52, line 24; Applicants note this amendment is in line 9 not 8

p. 11, line 17 – typographical correction of “epithelial ovarian cancer (EOC)”, see p. 3, line 10 for support; Applicants note this correction is in line 18 not 17

p. 12, line 22 – please cancel replacement of “that is not anchored to the membrane of a cell” with “that does not harbor a transmembrane domain”; Applicants note this occurs in line 23 not 22

p. 12, line 24 – please cancel replacement of “organism” with “cell” and addition of “through a constituent peptide domain. However, sErbB1 may be embedded or attached to the cell membrane through other moieties such as lipids, carbohydrates, and/or proteins.” Applicants note this occurs in line 25 not 24.

p. 13, line 3- please cancel replacement of “EGFR” with “sEGFR”

p. 13, line 6- please cancel addition of “or transformed” after “natural”; Applicants note this occurs in line 7 not 6.

p. 13, line 21 – replacement of “mice” with “mouse” is a grammatical correction; Applicants note this occurs in line 22 not 21.

p. 14, line 21 – replacement of “ErbB1” with “EGFR/ErbB1”; see p.2, lines 4 and 8 (ErbB1 and EGFR are the same gene); Applicants note this occurs in line 22 not 21

p. 14, line 23 – please cancel addition of “the full-length transcript” after “but”; Applicants note this occurs in line 24 not 23.

p. 17, line 2 – amendment to “epidermal growth factor receptor” is a typographical correction; epidermal growth factor receptor (EGFR) is used throughout, including this same paragraph at line 6; Applicants note this correction occurs at line 4 not 2

p. 17, line 19 – please cancel replacement of ‘histological’ with “stage, grade, histological and molecular”; applicants note this is at line 21 not line 19

p. 17, line 24 – please cancel replacement of “DNA” with “cDNA”; Applicants believe this refers to p. 18, line 2 instead of p. 17, line 24.

p. 18, line 5 – please cancel deletion of “inactive”; Applicants note this is line 7 not 5.

p. 18, line 6 – please cancel replacement of “EGFR” with “ErbB family members”; Applicants believe this refers to line 8 not 6.

p. 18, line 6 – please cancel replacement of “EGFR” with “ErbB receptors”; Applicants believe this refers to line 8 not 6

p. 18, line 7 – please cancel replacement of “EGFR” with “receptor”; Applicants believe this refers to line 9 not 7

p. 18, line 8 – please cancel replacement of “activity of the EGFR” with “and other signaling activities of ErbB receptor tyrosine kinases”; Applicants note this is line 10 not 8

p. 18, line 16 – please cancel replacement of “DNA” with “cDNA”; Applicants note this is line 18 not 16

p. 25, line 15 – please cancel addition of “cellular”; Applicants are unsure of the correct line number

p. 30, line 11- typographical correction of “sEGFR” with support within the sentence “By utilizing a portion of the sEGFR sequence... of the disclosed EGFR proteins...” It is apparent that EGFR should be sEGFR.

p. 31, line 1 – please cancel addition of “a peptide encoded by” after “e.g.”

p. 31, line 12 – please cancel addition of “sEGFR” after p110

p. 32, line 22 – please cancel addition of “saliva, sputum, breast nipple aspirates”

p. 34, line 5 – please cancel removal of “below”; Applicants believe this is line 6 not 5

p. 34, line 17 – please cancel replacement of “c-erbB1” with “EGFR/ErbB1”; Applicants believe this is line 18 not 17

p. 34, line 22 – Applicants believe the replacement of “1” with “2” is in line 23; Figure 1 should be Figure 2 (see Figures 1 and 2 for support)

p. 35, line 1 – replacement of “1986” to “2086” is a typographical correction of the base pairs for the 20 base pair reverse primer; Applicants note this is line 2 not 1

p. 35, line 17 – please cancel replacement of “represented” with “encoding” and “cDNA” with “sEGFR”

p. 35, line 25 - please cancel replacement of “EX15F and EX15R” with pEX15F (SEQ ID NO: 9) and pEX15BR (SEQ ID NO: 13)

p. 36, line 2 – please cancel deletion of “RNA represented by”

p. 36, line 4 – please cancel addition of “alternative” after “3.0 kb”

p. 36, line 13 – please cancel deletion of “(p110)(SEQ ID NO: 1)

p. 36, line 13 and p. 36, line 14 – typographical correction, “amino acids” is repeated

p. 36, line 24 – please cancel replacement of “c-erbB1” with “EGFR/ErbB1”

p. 36, line 25 – please cancel replacement of “transcript” with “EGFR/ErbB1”

p. 37, line 1 – please cancel replacement of “681” with “705”

p. 37, line 1 – please cancel deletion of “after cleavage of the signal peptide”

p. 37, line 5 – the addition “plus an additional 78 unique carboxy-terminal amino acids” after “EGFR” is supported on p. 10, line 14

p. 37, line 5 – please cancel addition of “plasmid” before “pDR2241”

p. 37, line 6 – please cancel replacement of “sErbB1” with “EGFR/ERBB1”, replacement of “encodes” with “synthesizes”, and replacement of “polypeptide (p110) that has ErbB1 ligand binding subdomains I through IV plus an additional 78 unique carboxy-terminal amino acids” with “glycosylated polypeptide (p110 sErbB1)”

p. 37, line 14 – typographical correction of “ μ Ci/ml of [35 S]”

p. 38, line 1 – please cancel addition of “cell lysates from” before “transfected”; Applicants note this is line 2 not 1

p. 38, line 5 – please cancel replacement of “mammalian” with “eukaryotic”; Applicants note this is line 6 not 5

p. 38, line 10 – replacement of “c-erbB1” with “ErbB1” is a typographical correction of the gene name to the corresponding protein name used in this context for receptors; see line 14 for support

p. 38, line 26 – please cancel replacement of “produces” with “encodes”; Applicants note this should be line 27 not 26

p. 39, line 9 – deletion of “(Figure 7A)”; Figure 7 relates to the ALISA described on p. 48, line 24 and should be deleted on p. 39, line 10 (not line 9)

p. 39, line 18 – please cancel addition of “may” before “route” and replacement of “and that” with “whereas”; Applicants note this should be line 20 not 18

p. 39, line 19 – please cancel replacement of “will” with “may”; Applicants note this should be line 21 not 19

p. 40, lines 4, 5, and 6 – please cancel deletion of “Cultures of ovarian carcinoma cells exposed to sEGFR preparations have reduced growth rates compared to cells which are not exposed to sEGFR. Thus, sEGFR can inhibit carcinoma cell proliferation.” Applicants note this should be lines 6, 7, and 8 instead of 4, 5 and 6.

p. 40, line 24 – replacement of “(MAb)” with “(MAbs)” is a typographical correction to make plural; Applicants note this should be p. 41, line 1 instead of p. 40, line 24.

p. 41, line 4 – replacement of “compete” with “complete” is obviously a typographical error as used in the context within this sentence; Applicants note this correction is in line 6 not 4

p. 41, line 15 – please cancel deletion of “(MAbs)”; Applicants note this is line 17 not 15

p. 41, line 23 – please cancel replacement of “ErbB1” with “sErbB1”; Applicants believe this should be line 25 not 23

p. 41, line 25 – please cancel replacement of “ErbB1” with “sErbB1”; Applicants believe this should be p. 42, line 2 instead of p. 41, line 25

p. 42, line 5 – please cancel the Accession Nos; Applicants note that this is line 7 not 5

p. 43, line 8 – please cancel replacement of “as well as to demonstrate that serum samples of healthy men and women contain a sErbB1 analog of approximately 110 kD (see Figure 14)” with “and in patients with ovarian cancer”.

p. 44, line 19 – please cancel replacement of “c-erbB1” with “EGFR/ERBB1”

p. 44, line 24 - please cancel replacement of “c-erbB1” with “EGFR/ERBB1”; Applicants note this is line 25 not 24

p. 45, line 1 - please cancel replacement of “c-erbB1” with “EGFR/ERBB1”; Applicants note this is line 2 not 1

p. 45, line 6 - please cancel replacement of “c-erbB1” with “EGFR/ERBB1”

p. 45, line 7- please cancel replacement of “c-erbB1” with “EGFR/ERBB1”

p. 45, line 8 - please cancel replacement of “c-erbB1” with “EGFR/ERBB1”

p. 45, line 10 - please cancel replacement of “c-erbB1” with “EGFR/ERBB1”

p. 45, line 14 – please cancel replacement of “(648)” with “(G418)”

p. 46, line 20 – replacement of “FPLCO” with “FPLC” is a typographical correction of an acronym; see the full name within the sentence: Fast Performance Liquid Chromatography

p. 47, lines 10 and 11 – replacement of “FPLCO” with “FPLC” is a typographical correction of an acronym (see above)

p. 49, line 1 – replacement of “the subdomain” with “subdomain IV” is a typographical correction; see beginning of the sentence at p. 48, line 25

p. 51, line 17 – please cancel replacement of “ALISA, believed to be the same 110 kD protein isolated from a human placental cDNA library as described above and is comprised of the 110 kD p110 sErbB1 SEQ ID NO. 2, and its variants” with “ALISA. Microsequence analysis of partially pure p110 sErbB1 from human serum using Matrix Assisted Laser Desorption/Ionization- Time of Flight Mass Spectrometry shows that this protein is derived from the 3.0 kb alternative transcript having SEQ ID NO. 2 of the invention.”

p. 52, line 1 – please cancel replacement of “appears to be less sensitive and accurate than the” with “differs substantially from the”; Applicants note this is line 14 not 1

p. 53, line 10 – please cancel replacement of “00” with “60”; Applicants note this is line 12 not 10

p. 53, line 12- please cancel replacement of “< or > 00 IU/L, and LH level < or > 00 IU/L” with “<30 IU/L (premenopause) or > 36 IU/L (postmenopause)”; Applicants note this is line 14 not 12

p. 59, line 3 – replacement of “(ú)” with (ω) is a typographical correction; Applicants note this occurs in line 4 not 3; see same sentence “the omega site”

p. 59, line 6 – please cancel replacement of ‘Table 4’ with “Table 2”; Applicants note this is line 7 not 6

p. 63, line 18 – please cancel replacement of “Atairgin” with “TBIG”; Applicants note this is on p. 60 not p. 63 and is within the original sequence listing.

Applicants respectfully request reconsideration of the objection.

III. Claim Rejections – 35 U.S.C. § 112, first paragraph

Applicants have amended claim 24 by removing “saliva.” The claim is now as it was previously presented. Applicants respectfully request removal of the rejection.

III. Claim Rejections – 35 U.S.C. § 103

Applicants have submitted a request to correct inventorship pursuant to 37 C.F.R. § 1.48(b). After careful consideration, it has been determined that Jill L. Reiter is not an inventor of the claims now pending (claims 18-32) in the instant application.

The Examiner has rejected claims 18-32 under 35 U.S.C. 103(a) as being obvious over Baron et al. (Journal of Immunol. Methods, 1998, 219: 23-43) in view of Baron et al. (Proceeding of the American Association of Cancer Research, Annual Meeting, March 1999, 40:43, Abstract #237). Applicants respectfully submit that both these references were published within one year of the filing date of the priority application, U.S. Provisional Application No. 60/157,144 filed September 30, 1999, and are their own work. Thus, the references are not statutory bar references under 35 U.S.C. §102. The MPEP states that “Unless it is a statutory bar, a rejection based on a publication may be overcome by a showing that it was published by applicant himself/herself ... See MPEP § 716.10 regarding 37 CFR 1.132 affidavits submitted to

show that the reference is a publication of applicant's own invention." *See* MPEP 715.01(c).

Andre T. Baron and Nita J. Maihle are both primary authors on the publication and the abstract and the only inventors of the current pending claims in the instant application. *See* Declaration of Dr. Andre Baron, Appendix B, ¶¶ 5 and 6.

The other authors on the cited disclosures are not inventors of the claimed invention. *See* Declaration of Dr. Andre Baron ¶ 6. The cited disclosures were a research publication and abstract of Applicants' own work. It is not uncommon for students and technicians or other collaborators who are involved in assaying and testing to be added as authors on such research abstracts and publications but who are not co-inventors on a patent application. *See* MPEP 715.01(c) and *In re Katz*, 687 F. 2d 450. This is similar to *In re Katz*, where the court held that the Applicant's disclosure of his or her own work within one year of the filing date cannot be used against him or her under 35 U.S.C. 102(a). 687 F. 2d 450. *See also* MPEP 715.01(c) and 2132.01.

The Declaration by Dr. Andre T. Baron establishes Dr. Andre T. Baron and Dr. Nita J. Maihle as sole inventors and that the 1998 publication and the 1999 abstract describe their own work. As such, Applicants respectfully request reconsideration of the rejection.

IV. Double Patenting

The Examiner has provisionally rejected claims 18-32 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-49 of copending Application No. 12/206,445. Applicants agree to file a terminal disclaimer in compliance with 37 C.F.R. 1.321 (c) upon allowance of the claims at issue.

V. Conclusion

Applicants respectfully submit that the application and claims are in condition for allowance. Accordingly, reconsideration and allowance of all claims are respectfully requested.

The Commissioner is hereby authorized to charge Deposit Account No. 03-2026 for any fees associated with this amendment or credit any overpayments.

Applicants would appreciate a telephone call to the undersigned attorney of record should the Examiner have any questions or comments with respect to this response for purposes of efficiently resolving same.

Respectfully submitted,

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